

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB2004/004054

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7	C12N15/85	C12N5/10	A01K67/027	C12N9/16	C07K14/59
	C12N9/18	G01N33/50	A61K49/00		

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K A01K C12N G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00/79264 A (TSAI TING FEN ; BAYLOR COLLEGE MEDICINE (US); ZOGHBI HUDA Y (US); CHEN) 28 December 2000 (2000-12-28) page 16, line 18 – page 17, line 10	13,14, 24,25
A	----- US 5 837 462 A (BAASNER SILKE ET-AL) 17 November 1998 (1998-11-17)  figure 1 examples 4,6,7 -----	1-10,15, 19-33
X	----- -/-	1-6,9, 19,20, 26-33

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

11 April 2005

Date of mailing of the international search report

02 MAY 2005

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PUTTINI S ET AL: "TETRACYCLINE-INDUCIBLE GENE EXPRESSION IN CULTURED RAT RENAL CD CELLS AND IN INTACT CD FROM TRANSGENIC MICE"            AMERICAN JOURNAL OF PHYSIOLOGY: RENAL, FLUID AND ELECTROLYTE PHYSIOLOGY, AMERICAN PHYSIOLOGICAL SOCIETY, US,            vol. 281, no. 6,            30 August 2001 (2001-08-30), pages F1164-F1172, XP001153223            ISSN: 0363-6127            figures 1,3,5            page F1165, right-hand column</p> <p>-----</p>	1-6, 9, 19, 20, 26-33
X	<p>CHANG KEEJONG ET AL: "Effective generation of transgenic pigs and mice by linker based sperm-mediated gene transfer."            BMC BIOTECHNOLOGY 'ELECTRONIC RESOURCE!'.            19 APR 2002,            vol. 2, no. 1, 19 April 2002 (2002-04-19),            pages 1-13, XP002311420            ISSN: 1472-6750</p> <p>page 4, right-hand column            page 10, paragraph 1 ..            table 2</p> <p>-----</p>	1-6, 9, 19-23, 26-33
Y	<p>BAO RUDI ET AL: "Activation of cancer-specific gene expression by the survivin promoter."            JOURNAL OF THE NATIONAL CANCER INSTITUTE.            3 APR 2002,            vol. 94, no. 7, 3 April 2002 (2002-04-03),            pages 522-528, XP002311421            ISSN: 0027-8874            figure 3            table 1</p> <p>-----</p>	10, 24, 25
X	<p>WANG MANPING ET AL: "MUSEAP, a novel reporter gene for the study of long-term gene expression in immunocompetent mice"            GENE (AMSTERDAM),            vol. 279, no. 1,            14 November 2001 (2001-11-14), pages 99-108, XP004324228            ISSN: 0378-1119            figure 1</p>	1-6, 9, 19, 20, 26-33
X	<p>&amp; WO 02/095068 A (AVENTIS PHARMA SA ;            ORSINI CECILE (FR); THUILLIER (FR); WANG            MANPING () 28 November 2002 (2002-11-28)            figure 1</p> <p>-----</p>	1-6, 9, 19, 20, 26-33
		-/-

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**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JAIN RENU K ET AL: "Aggregation chaperones enhance aggregation and storage of secretory proteins in endocrine cells" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 35, 1 September 2000 (2000-09-01), pages 27032-27036, XP002311422 ISSN: 0021-9258 abstract	1-9, 19, 20, 26-33
X	MEANS ROBERT E ET AL: "Neutralization sensitivity of cell culture-passaged simian immunodeficiency virus" JOURNAL OF VIROLOGY, vol. 71, no. 10, 1997, pages 7895-7902, XP002311423 ISSN: 0022-538X figure 1	1-6, 9, 19, 20, 26-33
X	BETTAN MICKAEL ET AL: "Secreted human placental alkaline phosphatase as a reporter gene for in vivo gene transfer" ANALYTICAL BIOCHEMISTRY, vol. 271, no. 2, 1 July 1999 (1999-07-01), pages 187-189, XP002191938 ISSN: 0003-2697 the whole document	1-10, 15, 19-33
Y	DEY ANUP ET AL: "Tissue- and cell type-specific expression of cytochrome P450 1A1 and cytochrome P450 1A2 mRNA in the mouse localized in situ hybridization" BIOCHEMICAL PHARMACOLOGY, vol. 58, no. 3, 1 August 1999 (1999-08-01), pages 525-537, XP002311431 ISSN: 0006-2952 the whole document	10
A	NAYLOR LOUISE H: "Reporter gene technology: The future looks bright" BIOCHEMICAL PHARMACOLOGY, vol. 58, no. 5, 1 September 1999 (1999-09-01), pages 749-757, XP002902679 OXFORD, GB ISSN: 0006-2952 table 1	1-10, 15, 19-33
A	EP 0 327 960 A (HOFFMANN LA ROCHE) 16 August 1989 (1989-08-16) page 5, lines 12-17	1-10, 15, 19-33
	-/-	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	US 6 632 978 B1 (KAESLIN EDGAR ET AL) 14 October 2003 (2003-10-14) abstract -----	1-10, 15, 19-33
P, A	WO 2004/011676 A (CXR BIOSCIENCES LTD ; ROSLIN INST EDINBURGH (GB); WOLF CHARLES ROLAND) 5 February 2004 (2004-02-05) abstract -----	1-10, 15, 19-33
X	MATZUK MARTIN M ET AL: "Overexpression of human chorionic gonadotropin causes multiple reproductive defects in transgenic mice." BIOLOGY OF REPRODUCTION, vol. 69, no. 1, July 2003 (2003-07), pages 338-346, XP002311218 ISSN: 0006-3363 figure 1 table 1 -----	1-6, 11, 19-28
Y	RULLI SUSANA B ET AL: "Reproductive disturbances, pituitary lactotrope adenomas, and mammary gland tumors in transgenic female mice producing high levels of human chorionic gonadotropin" ENDOCRINOLOGY, vol. 143, no. 10, October 2002 (2002-10), pages 4084-4095, XP002321089 ISSN: 0013-7227 figure 1A page 4089, last paragraph - page 4092, line 2 -----	7, 8, 12-14
Y	HERMEKING H ET AL: "14-3-3 sigma is a p53-regulated inhibitor of G2/M progression" MOLECULAR CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 1, December 1997 (1997-12), pages 3-11, XP002107211 ISSN: 1097-2765 abstract -----	12
A	COLE LAURENCE A: "Immunoassay of human chorionic gonadotropin, its free subunits, and metabolites" CLINICAL CHEMISTRY, AMERICAN ASSOCIATION FOR CLINICAL CHEMISTRY, WINSTON, US, vol. 43, no. 12, December 1997 (1997-12), pages 2233-2243, XP002292499 ISSN: 0009-9147 figure 1 -----	24, 25
		-/-

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<b>C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
<b>Category</b>	<b>Citation of document, with indication, where appropriate, of the relevant passages</b>	<b>Relevant to claim No.</b>
E	<p>WO 2004/090532 A (CXR BIOSCIENCES LIMITED; WOLF, ROLAND; BROWN, KENNETH) 21 October 2004 (2004-10-21) page 13, line 29 - page 18, line 21 examples 1,2 figure 5</p> <p>-----</p>	<p>1-8, 11-15, 19-33</p>

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## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material
    - in written format
    - in computer readable form
  - c. time of filing/furnishing
    - contained in the international application as filed
    - filed together with the international application in computer readable form
    - furnished subsequently to this Authority for the purpose of search
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: —  
because they relate to subject matter not required to be searched by this Authority, namely:  
**Although claims 31-33 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
**1-8, 15, 19-33 (all partially); claims 9-14 (all complete)**
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-8,15,19-33 (all partially); claims 9,10 (all complete)

Relating to a nucleic acid construct encoding a secretable or excretable reporter protein, secreted placental alkaline phosphatase (SEAP); cells and non-human animals comprising said nucleic acid construct; use of said gene, cell or animal for detecting gene activation or in methods of screening.

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Invention 2: claims 1-8,15,19-33 (all partially); claims 11-14 (all complete)

Relating to a nucleic acid construct encoding a secretable or excretable reporter protein, human beta choriogonadotropin; cells and non-human animals comprising said nucleic acid construct; use of said gene, cell or animal for detecting gene activation or in methods of screening.

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Invention 3: claims 1-8,15,19-33 (all partially); claims 16 (complete)

Relating to a nucleic acid construct encoding a secretable or excretable reporter protein, follicle stimulating hormone (FSH); cells and non-human animals comprising said nucleic acid construct; use of said gene, cell or animal for detecting gene activation or in methods of screening.

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Invention 4: claims 1-8,15,19-33 (all partially); claim 17 (complete)

Relating to a nucleic acid construct encoding a secretable or excretable reporter protein, antibody gamma or light chain (Bence Jones) protein; cells and non-human animals comprising said nucleic acid construct; use of said gene, cell or animal for detecting gene activation or in methods of screening.

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Invention 5: claims 1-8,15,19-33 (all partially); claim 18 (complete)

Relating to a nucleic acid construct encoding a secretable or excretable reporter protein, feline urinary carboxylase; cells and non-human animals comprising said nucleic acid construct; use of said gene, cell or animal for detecting gene activation or in methods of screening.

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**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

# INTERNATIONAL SEARCH REPORT

## Information on patent family members

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Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0079264	A	28-12-2000	AU WO	5890400 A 0079264 A1		09-01-2001 28-12-2000
US 5837462	A	17-11-1998	DE DE EP JP	19542051 A1 59610844 D1 0773293 A2 9131184 A		15-05-1997 15-01-2004 14-05-1997 20-05-1997
WO 02095068	A	28-11-2002	EP CA WO EP JP US	1270739 A1 2448145 A1 02095068 A2 1417334 A2 2004536588 T 2003104422 A1		02-01-2003 28-11-2002 28-11-2002 12-05-2004 09-12-2004 05-06-2003
EP 0327960	A	16-08-1989	EP JP	0327960 A1 2005862 A		16-08-1989 10-01-1990
US 6632978	B1	14-10-2003	US	2004016012 A1		22-01-2004
WO 2004011676	A	05-02-2004	AU WO	2003251343 A1 2004011676 A2		16-02-2004 05-02-2004
WO 2004090532	A	21-10-2004	WO	2004090532 A1		21-10-2004

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